

PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE
(MBHB Case No. 02-728-B)

In re Application of:)
James McSwiggen et al.)
Serial No.: 10/607,933) Group Art Unit: TBA
Filed: June 27, 2003) Examiner: TBA
For: RNA Interference Mediated)
Treatment of Alzheimer's Disease)
Using Short Interfering Nucleic)
Acid (siRNA))

TRANSMITTAL LETTER

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

In regard to the above-identified patent application:

1. We are transmitting herewith the attached:
 - a) Transmittal Letter in Duplicate;
 - b) Information Disclosure Statement Under 37 C.F.R. §1.97(b);
 - c) PTO Form 1449; and
 - d) 235 Cited References.
2. GENERAL AUTHORIZATION: Please charge any additional fees or credit overpayments to the Deposit Account No. 13-2490. A duplicate copy of this sheet is enclosed.
3. CERTIFICATE UNDER 37 CFR 1.8: The undersigned hereby certifies that this Transmittal Letter and papers, as described in paragraph 1 hereinabove, are being deposited with the United States Postal Service, with sufficient postage as first-class mail in an envelope addressed to: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450, on November 5, 2003.

Respectfully submitted,

Anita J. Terpstra
Reg. No. 47,132

Dated: November 5, 2003



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INFORMATION DISCLOSURE STATEMENT

**Honorable Commissioner of Patents and Trademarks
P.O. Box 1450
Alexandria, VA 22313-1450**

Dear Sir:

Pursuant to 37 C.F.R. Section 1.97 - 1.99, the Applicant wishes to make the following references of record in the above-identified application. This Information Disclosure Statement is in compliance with the continuing duty of candor as set forth in 37 C.F.R. Section 1.56. Copies of the cited references are enclosed. These references are also listed on the enclosed PTO Form 1449.

In the judgment of the undersigned, portions of the listed references may be material to the Examiner's consideration of the presently pending claims. This statement is not a representation that the listed references have effective dates early enough to be "prior art" within the meaning of 35 U.S.C. Section 102 or Section 103.

Applicants do not believe any fee is due with this submission. If this belief is in error and the Patent Office determines that the fee prescribed in the relevant portion of 37 C.F.R. Section

1.97 is applicable, the undersigned attorney by his signature hereby authorizes any such fee to be debited from Deposit Account 13-2490.

PATENT APPLICATION DOCUMENTS

1. McSwiggen, et al., Patent Application No. 10/444,853, filed May 23, 2003.
2. McSwiggen, et al., Patent Application No. PCT/US03-05346, filed February 20, 2003.
3. McSwiggen, et al., Patent Application No. PCT/US03/05028, filed February 20, 2003.
4. Blatt, et al., Patent Application No. 09/930,423, filed August 15, 2001.
5. McSwiggen, et al., Patent Application No. PCT/US03/04710, filed February 18, 2003.
6. McSwiggen, et al., Patent Application No. 10/205,309, filed July 25, 2002.
7. Beigelman, et al., Patent Application No. 60/358,580, filed February 20, 2002.
8. Beigelman, et al., Patent Application No. 60/363,124, filed March 11, 2002.
9. Beigelman, et al., Patent Application No. 60/286,782, filed June 6, 2002.
10. Beigelman, et al., Patent Application No. 60/406,784, filed August 29, 2002.
11. Beigelman, et al., Patent Application No. 60/408,378, filed September 5, 2002.
12. Beigelman, et al., Patent Application No. 60/409,293, filed September 2, 2002.
13. Beigelman, et al., Patent Application No. 60/440,129, filed January 15, 2003.
14. Beigelman, et al., Patent Application No. 60/082,404, filed April 20, 1998.
15. Vargeese, et al., Patent Application No. 10/427,160, filed April 30, 1998.
16. Vargeese, et al., Patent Application No. 10/201,394, filed July 22, 2002.
17. Usman, et al., Patent Application No. 60/402,992, filed August 13, 2002.
18. Vargeese, et al., Patent Application No. 10/201,394, filed August 13, 2001.
19. Matulic-Adamic, et al., Patent Application No. 60/362,016, filed March 6, 2002.

U. S. PATENTS

20. Sproat, et al., U.S. Patent No. 5,334,711, issued August 2, 1994.
21. Noonberg, et al., U.S. Patent No. 5,624,803, issued April 29, 1997.
22. Usman, et al., U.S. Patent No. 5,627,053, issued May 6, 1997.
23. Usman, et al., U.S. Patent No. 5,631,360, issued May 20, 1997.
24. Eckstein, et al., U.S. Patent No. 5,672,695, issued September 30, 1997.
25. Beigelman, et al., U.S. Patent No. 5,716,824, issued February 10, 1998.
26. Usman, et al., U.S. Patent No. 5,804,683, issued September 8, 1998.
27. Usman, et al., U.S. Patent No. 5,831,071, issued November 3, 1998.
28. Sullenger, et al., U.S. Patent No. 5,854,038, issued December 29, 1998.
29. Scaringe, et al., U.S. Patent No. 5,889,136, issued March 30, 1999.
30. Thompson, et al., U.S. Patent No. 5,902,880, issued May 11, 1999.
31. Matulic-Adamic, et al., U.S. Patent No. 5,998,203, issued December 7, 1999.
32. Brennan, et al., U.S. Patent No. 6,001,311, issued December 14, 1999.
33. Scaringe, et al., U.S. Patent No. 6,008,400, issued December 28, 1999.
34. Bellon, et al., U.S. Patent No. 6,054,576, issued April 25, 2000.
35. Scaringe, et al., U.S. Patent No. 6,111,086, issued August 29, 2000.
36. Usman, et al., U.S. Patent No. 6,117,657, issued September 12, 2000.
37. Thompson, et al., U.S. Patent No. 6,146,886, issued November 14, 2000.
38. Bellon, et al., U.S. Patent No. 6,162,909, issued December 19, 2000.
39. Matulic-Adamic, et al., U.S. Patent No. 6,248,878, issued June 19, 2001.
40. Gold, et al., U.S. Patent No. 6,300,074, issued October 9, 2001.
41. Bellon, et al., U.S. Patent No. 6,303,773, issued October 16, 2001.

42. Usman, et al., U.S. Patent No. 6,353,098, issued March 5, 2003.
43. Usman, et al., U.S. Patent No. 6,362,323, issued March 26, 2001.
44. Beigelman, et al., U.S. Patent No. 6,395,713, issued May 28, 2002.
45. Usman, et al., U.S. Patent No. 6,437,117, issued August 20, 2002.
46. Vook, et al., U.S. Patent No. 6,447,796, issued September 10, 2002.
47. Usman, et al., U.S. Patent No. 6,469,158, issued October 22, 2002.
48. Fire, et al., U.S. Patent No. 6,506,559, issued January 14, 2003.

FOREIGN PATENT DOCUMENTS

49. Patent No. 2,359,180, published August 3, 2000.
50. Patent No. WO 00/01846, published January 13, 2000.
51. Patent No. WO 00/44895, published August 3, 2000.
52. Patent No. WO 00/44914, published August 3, 2000.
53. Patent No. WO 00/53722, published September 14, 2000.
54. Patent No. WO/00/63364, published October 26, 2000.
55. Patent No. WO 00/66604, published November 9, 2000.
56. Patent No. WO 01/04313, published January 18, 2001.
57. Patent No. WO 01/16312, published March 8, 2001.
58. Patent No. WO 01/29058, published April 26, 2001.
59. Patent No. WO 01/36646, published May 21, 2001.
60. Patent No. WO 01/38551, published May 31, 2001.
61. Patent No. WO 01/42443, published June 14, 2001.
62. Patent No. WO 01/49844, published July 12, 2001.
63. Patent No. WO 01/53475, published July 26, 2001.

64. Patent No. WO 01/68836, published September 20, 2001.
65. Patent No. WO 01/70944, published September 27, 2001.
66. Patent No. WO 01/70949, published September 27, 2001.
67. Patent No. WO 01/72774, published October 4, 2001.
68. Patent No. WO 01/75164, published October 11, 2001.
69. Patent No. WO 01/92513, published May 29, 2001.
70. Patent No. WO 02/055692, published January 9, 2002.
71. Patent No. WO 02/055693, published January 9, 2002.
72. Patent No. WO 02/38805, published May 16, 2002.
73. Patent No. WO 02/44321, published June 6, 2002.
74. Patent No. WO 03/46185, published June 5, 2003
75. Patent No. WO 03/47518, published June 12, 2003
76. Patent No. WO 89/02439, published March 23, 1989.
77. Patent No. WO 92/07065, published April 20, 1992.
78. Patent No. WO 93/15187, published August 5, 1993.
79. Patent No. WO 93/23569, published November 25, 1993.
80. Patent No. WO 94/02595, published February 3, 1994.
81. Patent No. WO 95/06731, published March 9, 1995.
82. Patent No. WO 95/11910, published May 4, 1995.
83. Patent No. WO 96/10390, published April 11, 1996.
84. Patent No. WO 96/10391, published April 11, 1996.
85. Patent No. WO 96/10392, published April 11, 1996.
86. Patent No. WO 96/18736, published June 20, 1996.

87. Patent No. WO 97/26270, published July 24, 1997.
88. Patent No. WO 98/13526, published April 2, 1998.
89. Patent No. WO 99/07409, published February 18, 1999.
90. Patent No. WO 99/14226, published March 25, 1999.
91. Patent No. WO 99/31262, published June 24, 1999.
92. Patent No. WO 99/32619, published July 1, 1999.
93. Patent No. WO 99/49029, published September 30, 1999.
94. Patent No. WO 99/53050, published October 1, 1999.
95. Patent No. WO 99/54459, published October 28, 1999.

OTHER DOCUMENTS

96. Akhtar and Juliano, "Cellular Uptake and Intracellular Fate of AntiSense Oligonucleotides," Trends Cell Biol. 2:139-144 (1992)
97. Aldrian-Herrada et al., "A peptide nucleic acid (PNA) is more rapidly internalized in cultured neurons when coupled to a *retro-inverso* delivery peptide. The antisense activity depresses the target mRNA and protein in magnocellular oxytocin neurons," Nucleic Acids Research 26:4910-4916 (1998)
98. Allshire, "RNAi and Heterochromatin - A Hushed-up Affair," Science 297:1818-1819 (2002)
99. Andrews and Faller, "A rapid micropreparation technique for extraction of DNA-binding proteins from limiting numbers of mammalian cells," Nucleic Acids Research 19:2499 (1991)
100. Baenziger and Fiete, "Galactose and N-Acetylgalactosamine-Specific Endocytosis of Glycopeptides by Isolated Rat Hepatocytes," Cell 22:611-620 (1980)
101. Bahramian and Zarbl, 1999, Molecular and Cellular Biology, 19, 274-283.
102. Bass, "The short answer," Nature 411:428-429 (2001)
103. Beaucage and Iyer, "The Functionalization of Oligonucleotides Via Phosphoramidite Derivatives," Tetrahedron 49:1925-1963 (1993)
104. Beigelman et al., "Chemical Modification of Hammerhead Ribozymes," The Journal

of Biological Chemistry 270:25702-25708 (1995)

105. Bellon et al., "Post-synthetically Ligated Ribozymes: An Alternative Approach to Iterative Solid Phase Synthesis," Bioconjugate Chem. 8:204-212 (1997)
106. Bennett et al., "Cationic Lipids Enhance Cellular Uptake and Activity of Phosphorothioate Antisense Oligonucleotides," Mol. Pharmacology 41:1023-1033 (1992)
107. Berstein et al., 2001, *Nature*, 409, 363.
108. Boado et al., "Drug Delivery of Antisense Molecules to the Brain for Treatment of Alzheimer's Disease and Cerebral AIDS," *Journal of Pharmaceutical Sciences* 87:1308-1315 (1998)
109. Boado, "Antisense drug delivery through the blood-brain barrier," *Advanced Drug Delivery Reviews* 15:73-107 (1995)
110. Brennan et al., "Two-Dimensional Parallel Array Technology as a New Approach to Automated Combinatorial Solid-Phase Organic Synthesis," *Biotechnology and Bioengineering (Combinatorial Chemistry)* 61:33-45 (1998)
111. Brody and Gold, "Aptamers as therapeutic and diagnostic agents," *Reviews in Molecular Biotechnology* 74:5-13 (2000)+

112. Burgin et al., "Chemically Modified Hammerhead Ribozymes with Improved Catalytic Rates," Biochemistry 35:14090-14097 (1996) (volume no. mistakenly listed as 6)
113. Burlina et al., "Chemical Engineering of RNase Resistant and Catalytically Active Hammerhead Ribozymes," *Bioorganic & Medicinal Chemistry* 5:1999-2010 (1997)
114. Buxbaum et al., "Evidence that Tumor Necrosis Factor α Converting Enzyme is Involved in Regulated α -Secretase Cleavage of the Alzheimer Amyloid Protein Precursor," Jour. Biol. Chem. 273:27765-27767 (1998)
115. Caruthers et al., "Chemical Synthesis of Deoxyoligonucleotides and Deoxyoligonucleotide Analogs," Methods in Enzymology 211:3-19 (1992)
116. Chen et al., "Multitarget-Ribozyme Directed to Cleave at up to Nine Highly Conserved HIV-1 env RNA Regions Inhibits HIV-1 Replication-Potential Effectiveness Against Most Presently Sequenced HIV-1 Isolates," Nucleic Acids Research 20:4581-4589 (1992)
117. Chowrira et al., "*In Vitro* and *in Vivo* Comparison of Hammerhead, Hairpin, and

- Hepatitis Delta Virus Self-Processing Ribozyme Cassettes," J. Biol. Chem. 269:25856-25864 (1994)
118. Citron et al., "Mutation of the β -amyloid Precursor Protein in Familial Alzheimer's Disease Increases β -Protein Production," Nature 360:672-674 (1992)
 119. Cload and Schepartz, "Polyether Tethered Oligonucleotide Probes," J. Am. Chem. Soc. 113:6324-6326 (1991)
 120. Connolly et al., "Binding and Endocytosis of Cluster Glycosides by Rabbit Hepatocytes," The Journ. of Biol. Chem. 257:939-945 (1982)
 121. Conry et al., "Phase I Trial of a Recombinant Vaccinia Virus Encoding Carcinoembryonic Antigen in Metastatic Adenocarcinoma: Comparison of Intradermal versus Subcutaneous Administration," Clinical Cancer Research 5:2330-2337 (1999)
 122. Couture and Stinchcomb, "Anti-gene therapy: the use of ribozymes to inhibit gene function," Trends In Genetics 12:510-515 (1996)
 123. De Strooper et al., "A Presenilin-1-Dependent γ -Secretase-like Protease Mediates Release of Notch Intracellular Domain," Nature 398:518-522 (1999)
 124. De Strooper et al., "Deficiency of Presenilin-1 Inhibits the Normal Cleavage of Amyloid Precursor Protein," Nature 391:387-390 (1998)
 125. Dropulic et al., "Functional Characterization of a U5 Ribozyme: Intracellular Suppression of Human Immunodeficiency Virus Type I Expression," Journal of Virology 66:1432-1441 (1992)
 126. Durand et al., "Circular Dichroism Studies of an Oligodeoxyribonucleotide Containing a Hairpin Loop Made of a Hexaethylene Glycol Chain: Conformation and Stability," Nucleic Acids Research 18:6353-6359 (1990)
 127. Earnshaw et al., "Modified Oligoribonucleotides as Site-Specific Probes of RNA Structure and Function," Biopolymers 48:39-55 (1998)
 128. Elbashir et al., "Duplexes of 21-nucleotide RNAs mediate RNA interference in cultured mammalian cells," Nature 411:494-498 (2001)
 129. Elbashir et al., "Functional Anatomy of siRNAs for Mediating Efficient RNAi in *Drosophila Melanogaster* Embryo Lysate," The EMBO Journal 20:6877-6888 (2001)
 130. Elbashir et al., "RNA Interference is Mediated by 21- and 22-Nucleotide RNAs," Genes and Development 15:188-200 (2001)
 131. Elkins and Rossi, "Ch. 2 - Cellular Delivery of Ribozymes," in Delivery Strategies for

Antisense Oligonucleotide Therapeutics, edited by Akhtar, CRC Press, pp. 17-220 (1995)

132. Elroy-Stein and Moss, "Cytoplasmic Expression System Based on Constitutive Synthesis of Bacteriophage T7 RNA Polymerase in Mammalian Cells," Proc. Natl. Acad. Sci. USA 87:6743-6747 (1990)
133. Emerich et al., "Biocompatibility of Poly (DL-Lactide-co-Glycolide) Microspheres Implanted Into the Brain," Cell Transplantation 8:47-58 (1999)
134. Evin et al., 1999, Proc. Natl. Acad. Sci. U.S.A., 96, 3922
135. Ferentz and Verdine, "Disulfied Cross-Linked Oligonucleotides," J. Am. Chem. Soc. 113:4000-4002 (1991)
136. Fire et al., "Potent and Specific Genetic Interference by Double-Stranded RNA in *Caenorhabditis Elegans*," Nature 391:806-811(1998)
137. Fire, "RNA-triggered Gene Silencing," TIG 15:358-363(1999)
138. Freier et al., "Improved free-energy parameters for predictions of RNA duplex stability," Proc. Natl. Acad. Sci. USA 83:9373-9377 (1986) [sometimes referred to as Frier]
139. Games et al., "Alzheimer-Type Neuropathology in Transgenic Mice Overexpressing V717F β -Amyloid Precursor Protein," Nature 373:523-527 (1995)
140. Gao and Huang, "Cytoplasmic Expression of a Reporter Gene by Co-Delivery of T7 RNA Polymerase and T7 Promoter Sequence with Cationic Liposomes," Nucleic Acids Research 21:2867-2872 (1993)
141. Gold et al., "Diversity of Oligonucleotide Functions," Annu. Rev. Biochem. 64:763-797 (1995)
142. Gonzalez et al., "New Class of Polymers for the Delivery of Macromolecular Therapeutics," Bioconjugate Chem. 10:1068-1074 (1999)
143. Good et al., "Expression of small, therapeutic RNAs in human nuclei," Gene Therapy 4:45-54 (1997)
144. Hall et al., "Establishment and Maintenance of a Heterochromatin Domain," Science 297:2232-2237 (2002)
145. Hamilton et al., 1999, Science, 286, 950-951.
146. Hammond et al., "An RNA-Directed Nuclease Mediates Post-Transcriptional Gene Silencing in *Drosophila* Cells," Nature 404:293-296 (2000)

147. Hermann and Patel, "Adaptive Recognition by Nucleic Acid Aptamers," *Science* 287:820-825 (2000)
148. Hofland and Huang, "Formulation and Delivery of Nucleic Acids," *Handbook of Exp. Pharmacol.* 137:165-192 (1999)
149. Hunziker et al., "Nucleic Acid Analogues: Synthesis and Properties, in Modern Synthetic Methods," VCH, 331-417
150. Hutvagner and Zamore, "A MicroRNA in a Multiple-Turnover RNAi Enzyme Complex," Science 297:2056-2060 (2002)
151. Hutvagner et al., "A Cellular Function for the RNA-Interference Enzyme Dicer in the Maturation of the *let-7* Small Temporal RNA," Science 293:834-838 (2001)
152. Ishiwata et al., "Physical-Chemistry Characteristics and Biodistribution of Poly(ethylene glycol)-Coated Liposomes Using Poly(oxyethylene) Cholesteryl Ether," Chem. Pharm. Bull. 43:1005-1011 (1995) (mistakenly referred to as Ishiwataet)
153. Izant and Weintraub, "Constitutive and Conditional Suppression of Exogenous and Endogeneous Genes by Anti-Sense RNA," Science 229:345-352 (1985)
154. Jaschke et al., "Automated Incorporation of Polyethylene Glycol into Synthetic Oligonucleotides," Tetrahedron Letters 34:301-304 (1993)
155. Jayasena, "Aptamers: An Emerging Class of Molecules that Rival Antibodies in Diagnostics," *Clinical Chemistry* 45:1628-1650 (1999)
156. Jenuwein, "An RNA-Guided Pathway for the Epigenome," Science 297:2215-2218 (2002)
157. Jolliet-Riant and Tillement, "Drug transfer across the blood-brain barrier and improvement of brain delivery," *Fundam. Clin. Pharmacol.* 13:16-26 (1999)
158. Kang et al., "The Precursor of Alzheimer's Disease Amyloid A4 Protein Resembles a Cell-Surface Receptor," Nature 325:733-736 (1987)
159. Karpeisky et al, "Highly Efficient Synthesis of 2'-O-Amino Nucleosides And Their Incorporation in Hammerhead Ribozymes," Tetrahedron Letters 39:1131-1134 (1998)
160. Kashani-Sabet et al., "Reversal of the Malignant Phenotype by an Anti-ras Ribozyme," Antisense Research & Development 2:3-15 (1992)
161. Kusser, "Chemically modified nucleic acid aptamers for in vitro selections: evolving evolution," *Reviews in Molecular Biotechnology* 74:27-38 (2000)

162. Lammich et al., "Constitutive and Regulated α -Secretase Cleavage of Alzheimer's Amyloid Precursor Protein by a Disintegrin Metalloprotease," PNAS 96:3922-3927 (1999)
163. Lasic and Needham "The 'Stealth' Liposome: A Prototypical Biomaterial," Chemical Reviews 95:2601-2627 (1995)
164. Lasic and Papahadjopoulos, "Liposomes Revisited," Science 267:1275-1276 (1995)
165. Lee and Larson, "Modified Liposome Formulations for Cytosolic Delivery of Macromolecules," ACS Symposium Series 752:184-192 (2000)
166. Lee and Lee, "Preparation of Cluster Glycosides of N-Acetylgalactosamine That Have Subnanomolar Binding Constants Towards the Mammalian Hepatic Gal/GalNAc-specific Receptor," Glyconjugates J. 4:317-328 (1987)
167. Lee et al., "Expression of Small Interfering RNA's Targeted Against HIV-1 rev Transcripts in Human Cells," Nature Biotechnology 19:500-505 (2002)
168. L'Huillier et al., "Cytoplasmic Delivery of Ribozymes Leads to Efficient Reduction in α -Lactalbumin mRNA Levels in C1271 Mouse," EMBO J. 11:4411-4418 (1992)
169. Lieber et al., "Stable High-Level Gene Expression in Mammalian Cells by T7 Phage RNA Polymerase," Methods Enzymol. 217:47-66 (1993)
170. Limbach et al., "Summary: the modified nucleosides of RNA," Nucleic Acids Research 22(12):2183-2196 (1994)
171. Lin and Matteucci, "A Cytosine Analogue Capable of Clamp-Like Binding to a Guanine in Helical Nucleic Acid," J. Am. Chem. Soc. 120:8531-8532 (1998)
172. Lisziewicz et al., "Inhibition of Human Immunodeficiency Virus Type 1 Replication by Regulated Expression of a Polymeric Tat Activation Response RNA Decoy as a Strategy for Gene Therapy in AIDS," Proc. Natl. Acad. Sci. U.S.A. 90:8000-8004 (1993)
173. Liu et al., "Cationic Liposome-mediated Intravenous Gene Delivery," J. Biol. Chem. 270(42):24864-24870 (1995)
174. Loakes, "The Applications of Universal DNA Base Analogues," Nucleic Acids Research 29:2437-2447 (2001)
175. Ma et al., "Design and Synthesis of RNA Miniduplexes via a Synthetic Linker Approach. 2. Generation of Covalently Closed, Double-Stranded Cyclic HIV-1 TAR RNA Analogs with High Tat-Binding Affinity," Nucleic Acids Research 21:2585-2589 (1993)

176. Ma et al., "Design and Synthesis of RNA Miniduplexes via a Synthetic Linker Approach," Biochemistry 32:1751-1758 (1993)
177. Martinez et al., "Single-Stranded Antisense siRNAs Guide Target RNA Cleavage in RNAi," Cell 110:563-574 (2002)
178. Maurer et al., "Lipid-based systems for the intracellular delivery of genetic drugs," Molecular Membrane Biology 16:129-140 (1999)
179. McCurdy et al., "Deoxyoligonucleotides with Inverted Polarity: Synthesis and Use in Triple-Helix Formation" Nucleosides & Nucleotides 10:287-290 (1991)
180. McGarry and Lindquist, "Inhibition of heat shock protein synthesis by heat-inducible antisense RNA," Proc. Natl. Acad. Sci. USA 83:399-403 (1986)
181. McManus et al., "Gene Silencing Using Micro-RNA Designed Hairpins," RNA 8:842-850 (2002)
182. Mesmaeker et al, "Novel Backbone Replacements for Oligonucleotides," American Chemical Society, pp. 24-39 (1994)
183. Miyagashi and Taira, "U6 Promoter-driven siRNAs with Four Uridine 3' Overhangs Efficiently Suppress Targeted Gene Expression in Mammalian Cells," Nature Biotechnology 19:497-500 (2002)
184. Moore and Sharp, "Site-Specific Modification of Pre-mRNA: The 2'-Hydroxyl Groups at the Splice Sites," Science 256:992-996 (1992)
185. Noonberg et al., *In vivo* generation of highly abundant sequence-specific oligonucleotides for antisense and triplex gene regulation," Nucleic Acids Research 22(14):2830-2836 (1994)
186. Novina et al., "siRNA-Directed Inhibition of HIV-1 Infection," Nature Medicine 1-6 (2002)
187. Nykanen et al., "ATP Requirements and Small Interfering RNA Structure in the RNA Interference Pathway," Cell 107:309-321 (2001)
188. Ohkawa et al., "Activities of HIV-RNA Targeted Ribozymes Transcribed From a 'Shot-Gun' Type Ribozyme-trimming Plasmid," Nucleic Acids Symp. Ser. 27:15-16 (1992)
189. Ojwang et al., "Inhibition of Human Immunodeficiency Virus Type 1 Expression by a Hairpin Ribozyme," Proc. Natl. Acad. Sci. USA 89:10802-10806 (1992)
190. Oku et al., "Real-time analysis of liposomal trafficking in tumor-bearing mice by use of positron emission tomography," Biochimica et Biophysica Acta 1238:86-90

(1995)

191. Ono et al., "DNA Triplex Formation of Oligonucleotide Analogues Consisting of Linker Groups and Octamer Segments That Have Opposite Sugar-Phosphate Backbone Polarities," Biochemistry 30:9914-9921 (1991)
192. Pardridge et al., "Vector-mediated delivery of a polyamide ("peptide") nucleic acid analogue through the blood-brain barrier *in vivo*," Proc. Natl. Acad. Sci. USA 92:5592-5596 (1995)
193. Parrish, "Functional Anatomy of a dsRNA Trigger: Differential Requirement for the Two Trigger Strands in RNA Interference," Molecular Cell 6:1077-1087 (2000)
194. Paul et al., "Effective Expression of Small Interfering RNA in Human Cells," Nature Biotechnology 20:505-508 (2002)
195. Perreault et al., "Mixed Deoxyribo- and Ribo-Oligonucleotides with Catalytic Activity," Nature 344:565-567 (1990) (often mistakenly listed as Perrault)
196. Pieken et al., "Kinetic Characterization of Ribonuclease-Resistant 2'-Modified Hammerhead Ribozymes," Science 253:314-317 (1991)
197. Ponpipom et al., "Cell-Specific Ligands for Selective Drug Delivery to Tissues and Organs," J. Med. Chem. 24:1388-1395 (1981)
198. Reinhart and Bartel, "Small RNAs Correspond to Centromer Heterochromatic Repeats," Science 297:1831 (2002)
199. Reinhart et al., "MicroRNAs in Plants," Genes & Development 16:1616-1626 (2002)
200. Richardson and Schepartz, "Tethered Oligonucleotide Probes. A Strategy for the Recognition of Structured RNA," J. Am. Chem. Soc. 113:5109-5111 (1991)
201. Saenger (ed), "Modified Nucleosides and Nucleotides; Nucleoside Di- and Triphosphates; Coenzymes and Antibiotics, (ch.7)" Principles of Nucleic Acid Structure 158-200 (1984)
202. Sarver et al., "Ribozymes as Potential Anti-HIV-1 Therapeutic Agents" Science 247:1222-1225 (1990)
203. Scanlon et al., "Ribozyme-Mediated Cleavage of c-fos mRNA Reduces Gene Expression of DNA Synthesis Enzymes and Metallothionein," Proc. Natl. Acad. Sci. USA 88:10591-10595 (1991)
204. Scaringe et al., "Chemical synthesis of biologically active oligoribonucleotides using β -cyanoethyl protected ribonucleoside phosphoramidites," Nucl. Acids Res. 18:5433-5441 (1990)

205. Schroeder et al., "Diffusion Enhancement of Drugs by Loaded Nanoparticles in Vitro," *Pro. Neuro-Psychopharmacol. & Biol. Psychiat.* 23:941-949 (1999) [sometimes cited by RPI as *Prog Neuropsychopharmacol Biol Psychiatry* 23:941-949, 1999]
206. Schwarz et al., "Evidence that siRNAs Function as Guides, Not Primers, in the *Drosophila* and Human RNAi Pathways," *Molecular Cell* 10:537-548 (2002)
207. Seela and Kaiser, "Oligodeoxyribonucleotides containing 1,3-propanediol as nucleoside substitute," *Nucleic Acids Research* 15:3113-3129 (1987)
208. Seela and Kaiser, *Nucleic Acids Res.* 1990, 18:6353
209. Shabarova et al., "Chemical ligation of DNA: The first non-enzymatic assembly of a biologically active gene," *Nucleic Acids Research* 19:4247-4251 (1991)
210. Sullenger and Cech, "Tethering Ribozymes to a Retroviral Packaging Signal for Destruction of Viral RNA," *Science* 262:1566-1569 (1993)
211. Sun, "Technology evaluation: SELEX, Giliad Sciences Inc," *Current Opinion in Molecular Therapeutics* 2:100-105 (2000)
212. Taira et al., "Construction of a novel RNA-transcript-trimming plasmid which can be used both *in vitro* in place of run-off and (G)-free transcriptions and *in vivo* as multi-sequences transcription vectors," *Nucleic Acids Research* 19:5125-5130 (1991)
213. Thompson et al., "Improved accumulation and activity of ribozymes expressed from a tRNA-based RNA polymerase III promoter," *Nucleic Acids Research* 23:2259-2268 (1995)
214. Turner et al., "Improved Parameters for Prediction of RNA Structure," *Cold Spring Harbor Symposia on Quantitative Biology* Volume LII, pp. 123-133 (1987)
215. Turner et al., "Free Energy Increments for Hydrogen Bonds in Nucleic Acid Base Pairs," *J. Am. Chem. Soc.* 109:3783-3785 (1987)
216. Tuschl et al., "Targeted mRNA Degradation by Double-Stranded RNA In Vitro," *Genes & Development* 3191-3197 (1999)
217. Tuschl, "RNA Interference and Small Interfering RNAs," *Chembiochem* 2:239-245 (2001)
218. Tyler et al., "Peptide nucleic acids targeted to the neuropeptides receptor and administered i.p. cross the blood-brain barrier and specifically reduce gene expression," *Proc. Natl. Acad. Sci. USA* 96:7053-7058 (1999)
219. Tyler et al., "Specific gene blockade shows that peptide nucleic acids readily enter

- neuronal cells *in vivo*," *FEBS Letters* 421:280-284 (1998)
220. Usman and Cedergren, "Exploiting the chemical synthesis of RNA," *TIBS* 17:334-339 (1992)
221. Usman et al., "Automated Chemical Synthesis of Long Oligoribonucleotides Using 2'-O-Silylated Ribonucleoside 3'-O-Phosphoramidites on a Controlled-Pore Glass Support: Synthesis of a 43-Nucleotide Sequence Similar to the 3'-Half Molecule of an *Escherichia coli* Formylmethionine tRNA," *J. Am. Chem. Soc.* 109:7845-7854 (1987)
222. Usman et al., "Chemical modification of hammerhead ribozymes: activity and nuclease resistance," *Nucleic Acids Symposium Series* 31:163-164 (1994)
223. Vassar et al., "β-Secretase Cleavage of Alzheimer's Amyloid Precursor Protein by the Transmembrane Aspartic Protease BACE," *Science* 286:735-741 (1999)
224. Ventura et al., "Activation of HIV-Specific Ribozyme Activity by Self-Cleavage," *Nucleic Acids Research* 21:3249-3255 (1993)
225. Verma and Eckstein, "Modified Oligonucleotides: Synthesis and Strategy for Users," *Annu. Rev. Biochem.* 67:99-134 (1998)
226. Volpe et al., "Regulation of Heterochromatic Silencing and Histone H3 Lysine-9 Methylation by RNAi," *Science* 297:1833-1837 (2002)
227. Weerasinghe et al., "Resistance to Human Immunodeficiency Virus Type 1 (HIV-1) Infection in Human CD4⁺ Lymphocyte-Derived Cell Lines Conferred by Using Retroviral Vectors Expressing an HIV-1 RNA-Specific Ribozyme," *Journal of Virology* 65:5531-5534 (1994)
228. Wianny and Zernicka-Goetz et al., "Specific Interference with Gene Function by Double-Stranded RNA in Early Mouse Development," *Nature Cell Biology* 2:70-75 (2000)
229. Wincott et al., "Synthesis, deprotection, analysis and purification of RNA and ribozymes," *Nucleic Acids Research* 23(14):2677-2684 (1995)
230. Wincott et al., "A Practical Method for the Production of RNA and Ribozymes," *Methods in Molecular Biology* 74:59-69 (1997)
231. Wolfe et al., "Two Transmembrane Aspartates in Presenilin-1 Required for Presenilin Endoproteolysis and γ-Secretase Activity," *Nature* 398:513-517 (1999)
232. Wu and Wu, "Receptor-mediated *in Vitro* Gene Transformation by a Soluble DNA Carrier System," *The Journ. of Biol. Chem.* 262:4429-4432 (1987)
233. Yu et al., "A Hairpin Ribozyme Inhibits Expression of Diverse Strains of Human

Immunodeficiency Virus Type 1," Proc. Natl. Acad. Sci. USA 90:6340-6344 (1993)

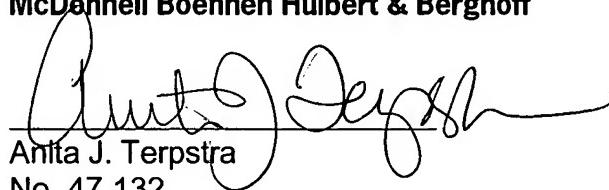
234. Zamore et al., "RNAi: Double-Stranded RNA Directs the ATP-Dependent Cleavage of mRNA at 21 to 23 Nucleotide Intervals," Cell 101:25-33 (2000)
235. Zhou et al., "Synthesis of Functional mRNA in Mammalian Cells by Bacteriophage T3 RNA Polymerase," Mol. Cell. Biol. 10:4529-4537 (1990)

Respectfully submitted,
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PATENT & TRADEMARK OFFICE

U.S. PATENT APPLICATION DOCUMENTS

Examiner Initial	No.	Document Number	Filing Date	Name	Publication Date if Appropriate
	1.	10/444,853	5/23/03	McSwiggen	
	2.	PCT/US03/05346	2/20/03	Simpson	
	3.	PCT/US03/05028	7/18/84	Sulzman	
	4.	09/930,423	8/15/01	Blatt	
	5.	PCT/US03/04710	1/23/84	Dial	
	6.	10/205,309	7/25/02	McSwiggen	
	7.	60/358,580	2/20/02	Beigelman	
	8.	60/363,124	3/11/02	Beigelman	
	9.	60/386,782	6/6/02	Beigelman	
	10.	60/406,784	8/29/02	Beigelman	
	11.	60/408,378	9/5/02	Beigelman	
	12.	60/409,293	9/2/02	Beigelman	
	13.	60/440,129	1/15/03	Jackson	
	14.	60/082,404	4/20/98	Blatt	
	15.	10/427,160	4/30/03	Vargeese	
	16.	10/201,394	7/22/02	Vargeese	
	17.	60/402,996	08/13/02	Usman	
	18.	10/201,394	8/13/01	Vargeese	
	19.	60/362,016	3/6/02	Matulic-Adamic	

U.S. PATENT DOCUMENTS

Examiner Initial	No.	Document Number	Date	Name	Class	Subclass	Filing Date
	20.	5,334,711	8/2/94	Sproat			
	21.	5,624,803	4/29/97	Noonberg			
	22.	5,627,053	5/6/97	Usman			
	23.	5,631,360	5/20/97	Usman			
	24.	5,672,695	9/30/97	Eckstein			
	25.	5,716,824	2/10/98	Beigelman			
	26.	5,804,683	9/8/98	Usman			
Examiner	Date Considered						

EXAMINER: Initial if citation considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with any communication.

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Examiner Initial	No.	Document Number	Date	Name	Class	Subclass	Filing Date
	27.	5,831,071	11/3/98	Usman			
	28.	5,854,038	12/29/98	Sullenger			
	29.	5,889,136	3/30/99	Scaringe			
	30.	5,902,880	5/11/99	Thompson			
	31.	5,998,203	12/7/99	Matulic-Adamic			
	32.	6,001,311	12/14/99	Brennan			
	33.	6,008,400	12/28/99	Scaringe			
	34.	6,054,576	4/25/00	Bellon			
	35.	6,111,086	8/29/00	Scaringe			
	36.	6,117,657	9/12/00	Usman			
	37.	6,146,886	11/14/00	Thompson			
	38.	6,162,909	12/19/00	Bellon			
	39.	6,248,878	6/19/01	Matulic-Adamic			
	40.	6,300,074	10/9/01	Gold			
	41.	6,303,773	10/16/01	Bellon			
	42.	6,353,098	3/5/03	Usman			
	43.	6,362,323	3/26/01	Usman			
	44.	6,395,713	5/28/02	Beigelman			
	45.	6,437,117	8/20/02	Usman			
	46.	6,447,796	9/10/02	Vook			
	47.	6,469,158	10/22/02	Usman			
	48.	6,506,559	1/14/03	Fire			

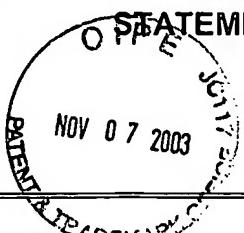
FOREIGN PATENT DOCUMENTS

Examiner Initial	No.	Document Number	Date	Country	Class	Subclass	Translation Yes	Translation No
	49.	2,359,180	8/3/00	Canada				
	50.	WO 00/01846	1/13/00	PCT				
	51.	WO 00/44895	8/3/00	PCT				
	52.	WO 00/44914	8/3/00	PCT				

Examiner	Date Considered

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Filing Date:

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Group:

Examiner Initial	No.	Document Number	Date	Country	Class	Subclass	Translation Yes	Translation No
	53.	WO 00/53722	9/14/00	PCT				
	54.	WO 00/63364	10/26/00	PCT				
	55.	WO 00/66604	11/9/00	PCT				
	56.	WO 01/04313	1/18/01	PCT				
	57.	WO 01/16312	3/8/01	PCT				
	58.	WO 01/29058	4/26/01	PCT				
	59.	WO 01/36646	5/25/01	PCT				
	60.	WO 01/38551	5/31/01	PCT				
	61.	WO 01/42443	6/14/01	PCT				
	62.	WO 01/49844	7/12/01	PCT				
	63.	WO 01/53475	7/26/01	PCT				
	64.	WO 01/68836	9/20/01	PCT				
	65.	WO 01/70944	9/27/01	PCT				
	66.	WO 01/70949	9/27/01	PCT				
	67.	WO 01/72774	10/4/01	PCT				
	68.	WO 01/75164	10/11/01	PCT				
	69.	WO 01/92513	6/12/01	PCT				
	70.	WO 02/055692	7/18/02	PCT				
	71.	WO 02/055693	7/18/02	PCT				
	72.	WO 02/38805	5/16/02	PCT				
	73.	WO 02/44321	6/6/02	PCT				
	74.	WO 03/46185	6/5/03	PCT				
	75.	WO 03/47518	6/12/03	PCT				
	76.	WO 89/02439	3/23/89	PCT				
	77.	WO 92/07065	4/30/92	PCT				
	78.	WO 93/15187	8/5/93	PCT				
	79.	WO 93/23569	11/25/93	PCT				
	80.	WO 94/02595	2/3/94	PCT				

Examiner

Date Considered

EXAMINER: Initial if citation considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with any communication.

Form PTO-1449

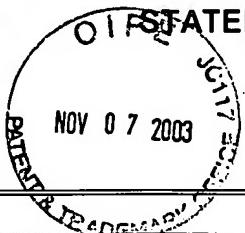
U.S. Department of Commerce
Patent and Trademark Office

Atty. Docket No.

Serial No.

02-728-B

10/607,933

**INFORMATION DISCLOSURE
STATEMENT BY APPLICANT**

Applicant: McSwiggen, et al.

Filing Date:
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Group:

Examiner Initial	No.	Document Number	Date	Country	Class	Subclass	Translation Yes	Translation No
	81.	WO 95/06731	3/9/95	PCT				
	82.	WO 95/11910	5/4/95	PCT				
	83.	WO 96/10390	4/11/96	PCT				
	84.	WO 96/10391	4/11/96	PCT				
	85.	WO 96/10392	4/11/96	PCT				
	86.	WO 96/18736	6/20/96	PCT				
	87.	WO 97/26270	7/24/97	PCT				
	88.	WO 98/13526	4/2/98	PCT				
	89.	WO 99/07409	2/18/99	PCT				
	90.	WO 99/14226	3/25/99	PCT				
	91.	WO 99/31262	6/24/99	PCT				
	92.	WO 99/32619	7/1/99	PCT				
	93.	WO 99/49029	9/30/99	PCT				
	94.	WO 99/53050	10/21/99	PCT				
	95.	WO 99/54459	10/28/99	PCT				

OTHER DOCUMENTS - Including Author, Title, Date, Pertinent Pages, Etc.

Examiner Initial	No.	
	96.	Akhtar and Juliano, "Cellular Uptake and Intracellular Fate of AntiSense Oligonucleotides," <i>Trends Cell Biol.</i> 2:139-144 (1992)
	97.	Aldrian-Herrada et al., "A peptide nucleic acid (PNA) is more rapidly internalized in cultured neurons when coupled to a <i>retro-inverso</i> delivery peptide. The antisense activity depresses the target mRNA and protein in magnocellular oxytocin neurons," <i>Nucleic Acids Research</i> 26:4910-4916 (1998)
	98.	Allshire, "RNAi and Heterochromatin - A Hushed-up Affair," <i>Science</i> 297:1818-1819 (2002)
	99.	Andrews and Faller, "A rapid micropreparation technique for extraction of DNA-binding proteins from limiting numbers of mammalian cells," <i>Nucleic Acids Research</i> 19:2499 (1991)

Examiner

Date Considered

EXAMINER: Initial if citation considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with any communication.

Form PTO-1449

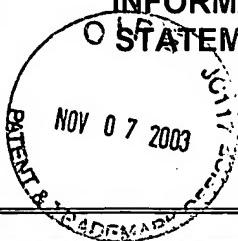
U.S. Department of Commerce
Patent and Trademark Office

Atty. Docket No.

Serial No.

02-728-B

10/607,933

**INFORMATION DISCLOSURE
STATEMENT BY APPLICANT**

Applicant: McSwiggen, et al.

Filing Date:

June 27, 2003

Group:

	100.	Benziger and Fiete, "Galactose and N-Acetylgalactosamine-Specific Endocytosis of Glycopeptides by Isolated Rat Hepatocytes," <i>Cell</i> 22:611-620 (1980)
	101.	Bahramian and Zarbl, 1999, <i>Molecular and Cellular Biology</i> , 19, 274-283.
	102.	Bass, "The short answer," <i>Nature</i> 411:428-429 (2001)
	103.	Beaucage and Iyer, "The Functionalization of Oligonucleotides Via Phosphoramidite Derivatives," <i>Tetrahedron</i> 49:1925-1963 (1993)
	104.	Beigelman et al., "Chemical Modification of Hammerhead Ribozymes," <i>The Journal of Biological Chemistry</i> 270:25702-25708 (1995)
	105.	Bellon et al., "Post-synthetically Ligated Ribozymes: An Alternative Approach to Iterative Solid Phase Synthesis," <i>Bioconjugate Chem.</i> 8:204-212 (1997)
	106.	Bennett et al., "Cationic Lipids Enhance Cellular Uptake and Activity of Phosphorothioate Antisense Oligonucleotides," <i>Mol. Pharmacology</i> 41:1023-1033 (1992)
	107.	Bernstein et al., "Role for a Bidentate Ribonuclease in the Initiation Step of RNA Interference," <i>Nature</i> 409:363-366 (2001)
	108.	Boado et al., "Drug Delivery of Antisense Molecules to the Brain for Treatment of Alzheimer's Disease and Cerebral AIDS," <i>Journal of Pharmaceutical Sciences</i> 87:1308-1315 (1998)
	109.	Boado, "Antisense drug delivery through the blood-brain barrier," <i>Advanced Drug Delivery Reviews</i> 15:73-107 (1995)
	110.	Brennan et al., "Two-Dimensional Parallel Array Technology as a New Approach to Automated Combinatorial Solid-Phase Organic Synthesis," <i>Biotechnology and Bioengineering (Combinatorial Chemistry)</i> 61:33-45 (1998)
	111.	Brody and Gold, "Aptamers as therapeutic and diagnostic agents," <i>Reviews in Molecular Biotechnology</i> 74:5-13 (2000)+
	112.	Burgin et al., "Chemically Modified Hammerhead Ribozymes with Improved Catalytic Rates," <i>Biochemistry</i> 35:14090-14097 (1996) (volume no. mistakenly listed as 6)
	113.	Burlina et al., "Chemical Engineering of RNase Resistant and Catalytically Active Hammerhead Ribozymes," <i>Bioorganic & Medicinal Chemistry</i> 5:1999-2010 (1997)
	114.	Buxbaum et al., "Evidence that Tumor Necrosis Factor α Converting Enzyme is Involved in Regulated α -Secretase Cleavage of the Alzheimer Amyloid Protein Precursor," <i>Jour. Biol. Chem.</i> 273:27765-27767 (1998)
	115.	Caruthers et al., "Chemical Synthesis of Deoxyoligonucleotides and Deoxyoligonucleotide Analogs," <i>Methods in Enzymology</i> 211:3-19 (1992)

Examiner

Date Considered

EXAMINER: Initial if citation considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with any communication.

Form PTO-1449

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02-728-B

10/607,933

**INFORMATION DISCLOSURE
STATEMENT BY APPLICANT**

Applicant: McSwiggen, et al.

Filing Date:
June 27, 2003

Group:

	116.	Chen et al., "Multitarget-Ribozyme Directed to Cleave at up to Nine Highly Conserved HIV-1 env RNA Regions Inhibits HIV-1 Replication-Potential Effectiveness Against Most Presently Sequenced HIV-1 Isolates," <u>Nucleic Acids Research</u> 20:4581-4589 (1992)
	117.	Chowrira et al., " <i>In Vitro</i> and <i>in Vivo</i> Comparison of Hammerhead, Hairpin, and Hepatitis Delta Virus Self-Processing Ribozyme Cassettes," <u>J. Biol. Chem.</u> 269:25856-25864 (1994)
	118.	Citron et al., "Mutation of the β -amyloid Precursor Protein in Familial Alzheimer's Disease Increases β -Protein Production," <u>Nature</u> 360:672-674 (1992)
	119.	Cload and Schepartz, "Polyether Tethered Oligonucleotide Probes," <u>J. Am. Chem. Soc.</u> 113:6324-6326 (1991)
	120.	Connolly et al., "Binding and Endocytosis of Cluster Glycosides by Rabbit Hepatocytes," <u>The Journ. of Biol. Chem.</u> 257:939-945 (1982)
	121.	Conry et al., "Phase I Trial of a Recombinant Vaccinia Virus Encoding Carcinoembryonic Antigen in Metastatic Adenocarcinoma: Comparison of Intradermal <i>versus</i> Subcutaneous Administration," <u>Clinical Cancer Research</u> 5:2330-2337 (1999)
	122.	Couture and Stinchcomb, "Anti-gene therapy: the use of ribozymes to inhibit gene function," <u>Trends In Genetics</u> 12:510-515 (1996)
	123.	De Strooper et al., "A Presenilin-1-Dependent γ -Secretase-like Protease Mediates Release of Notch Intracellular Domain," <u>Nature</u> 398:518-522 (1999)
	124.	De Strooper et al., "Deficiency of Presenilin-1 Inhibits the Normal Cleavage of Amyloid Precursor Protein," <u>Nature</u> 391:387-390 (1998)
	125.	Dropulic et al., "Functional Characterization of a U5 Ribozyme: Intracellular Suppression of Human Immunodeficiency Virus Type I Expression," <u>Journal of Virology</u> 66:1432-1441 (1992)
	126.	Durand et al., "Circular Dichroism Studies of an Oligodeoxyribonucleotide Containing a Hairpin Loop Made of a Hexaethylene Glycol Chain: Conformation and Stability," <u>Nucleic Acids Research</u> 18:6353-6359 (1990)
	127.	Earnshaw et al., "Modified Oligoribonucleotides as Site-Specific Probes of RNA Structure and Function," <u>Biopolymers</u> 48:39-55 (1998)
	128.	Elbashir et al., "Duplexes of 21-nucleotide RNAs mediate RNA interference in cultured mammalian cells," <u>Nature</u> 411:494-498 (2001)
	129.	Elbashir et al., "Functional Anatomy of siRNAs for Mediating Efficient RNAi in <i>Drosophila Melanogaster</i> Embryo Lysate," <u>The EMBO Journal</u> 20:6877-6888 (2001)

Examiner

Date Considered

EXAMINER: Initial if citation considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with any communication.

Form PTO-1449

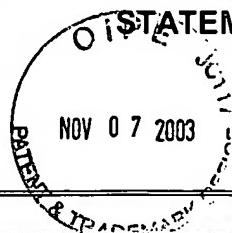
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02-728-B

10/607,933

INFORMATION DISCLOSURE
STATEMENT BY APPLICANT

Applicant: McSwiggen, et al.

Filing Date:

June 27, 2003

Group:

	130.	Elbashir et al., "RNA Interference is Mediated by 21- and 22-Nucleotide RNAs," <u>Genes and Development</u> 15:188-200 (2001)
	131.	Elkins and Rossi, "Ch. 2 - Cellular Delivery of Ribozymes," in <u>Delivery Strategies for Antisense Oligonucleotide Therapeutics</u> , edited by Akhtar, CRC Press, pp. 17-220 (1995)
	132.	Elroy-Stein and Moss, "Cytoplasmic Expression System Based on Constitutive Synthesis of Bacteriophage T7 RNA Polymerase in Mammalian Cells," <u>Proc. Natl. Acad. Sci. USA</u> 87:6743-6747 (1990)
	133.	Emerich et al., "Biocompatibility of Poly (DL-Lactide-co-Glycolide) Microspheres Implanted Into the Brain," <u>Cell Transplantation</u> 8:47-58 (1999)
	134.	Evin et al., "Constitutive and Regulated α -Secretase Cleavage of Alzheimer's Amyloid Precursor Protein by A Disintegrin Metalloprotease" 1999, Proc. Natl. Acad. Sci. U.S.A., 96, 3922
	135.	Ferentz and Verdine, "Disulfied Cross-Linked Oligonucleotides," <u>J. Am. Chem. Soc.</u> 113:4000-4002 (1991)
	136.	Fire et al., "Potent and Specific Genetic Interference by Double-Stranded RNA in <u>Caenorhabditis Elegans</u> ," <u>Nature</u> 391:806-811(1998)
	137.	Fire, "RNA-triggered Gene Silencing," <u>TIG</u> 15:358-363(1999)
	138.	Freier et al., "Improved free-energy parameters for predictions of RNA duplex stability," <u>Proc. Natl. Acad. Sci. USA</u> 83:9373-9377 (1986) [sometimes referred to as Frier]
	139.	Games et al., "Alzheimer-Type Neuropathology in Transgenic Mice Overexpressing V717F β -Amyloid Precursor Protein," <u>Nature</u> 373:523-527 (1995)
	140.	Gao and Huang, "Cytoplasmic Expression of a Reporter Gene by Co-Delivery of T7 RNA Polymerase and T7 Promoter Sequence with Cationic Liposomes," <u>Nucleic Acids Research</u> 21:2867-2872 (1993)
	141.	Gold et al., "Diversity of Oligonucleotide Functions," <u>Annu. Rev. Biochem.</u> 64:763-797 (1995)
	142.	Gonzalez et al., "New Class of Polymers for the Delivery of Macromolecular Therapeutics," <u>Bioconjugate Chem.</u> 10:1068-1074 (1999)
	143.	Good et al., "Expression of small, therapeutic RNAs in human nuclei," <u>Gene Therapy</u> 4:45-54 (1997)
	144.	Hall et al., "Establishment and Maintenance of a Heterochromatin Domain," <u>Science</u> 297:2232-2237 (2002)
	145.	Hamilton et al., "A Species of Small Antisense RNA in Posttranscriptional Gene Silencing in Plants" 1999, <u>Science</u> , 286, 950-951.

Examiner

Date Considered

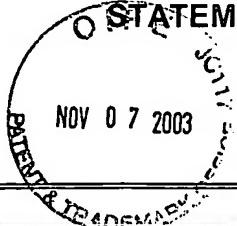
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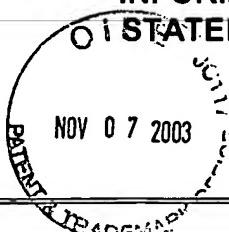
Group:

	146.	Hammond et al., "An RNA-Directed Nuclease Mediates Post-Transcriptional Gene Silencing in <i>Drosophila</i> Cells," <i>Nature</i> 404:293-296 (2000)
	147.	Hermann and Patel, "Adaptive Recognition by Nucleic Acid Aptamers," <i>Science</i> 287:820-825 (2000)
	148.	Hofland and Huang, "Formulation and Delivery of Nucleic Acids," <i>Handbook of Exp. Pharmacol.</i> 137:165-192 (1999)
	149.	Hunziker et al., "Nucleic Acid Analogues: Synthesis and Properties, in Modern Synthetic Methods," <i>VCH</i> , 331-417
	150.	Hutvagner and Zamore, "A MicroRNA in a Multiple-Turnover RNAi Enzyme Complex," <i>Science</i> 297:2056-2060 (2002)
	151.	Hutvagner et al., "A Cellular Function for the RNA-Interference Enzyme Dicer in the Maturation of the <i>let-7</i> Small Temporal RNA," <i>Science</i> 293:834-838 (2001)
	152.	Ishiwata et al., "Physical-Chemistry Characteristics and Biodistribution of Poly(ethylene glycol)-Coated Liposomes Using Poly(oxyethylene) Cholesteryl Ether," <i>Chem. Pharm. Bull.</i> 43:1005-1011 (1995) (mistakenly referred to as Ishiwataet)
	153.	Izant and Weintraub, "Constitutive and Conditional Suppression of Exogenous and Endogeneous Genes by Anti-Sense RNA," <i>Science</i> 229:345-352 (1985)
	154.	Jaschke et al., "Automated Incorporation of Polyethylene Glycol into Synthetic Oligonucleotides," <i>Tetrahedron Letters</i> 34:301-304 (1993)
	155.	Jayasena, "Aptamers: An Emerging Class of Molecules that Rival Antibodies in Diagnostics," <i>Clinical Chemistry</i> 45:1628-1650 (1999)
	156.	Jenuwein, "An RNA-Guided Pathway for the Epigenome," <i>Science</i> 297:2215-2218 (2002)
	157.	Jolliet-Riant and Tillement, "Drug transfer across the blood-brain barrier and improvement of brain delivery," <i>Fundam. Clin. Pharmacol.</i> 13:16-26 (1999)
	158.	Kang et al., "The Precursor of Alzheimer's Disease Amyloid A4 Protein Resembles a Cell-Surface Receptor," <i>Nature</i> 325:733-736 (1987)
	159.	Karpeisky et al, "Highly Efficient Synthesis of 2'-O-Amino Nucleosides And Their Incorporation in Hammerhead Ribozymes," <i>Tetrahedron Letters</i> 39:1131-1134 (1998)
	160.	Kashani-Sabet et al., "Reversal of the Malignant Phenotype by an Anti-ras Ribozyme," <i>Antisense Research & Development</i> 2:3-15 (1992)
	161.	Kusser, "Chemically modified nucleic acid aptamers for in vitro selections: evolving evolution," <i>Reviews in Molecular Biotechnology</i> 74:27-38 (2000)
	162.	Lammich et al., "Constitutive and Regulated α -Secretase Cleavage of Alzheimer's

Examiner

Date Considered

EXAMINER: Initial if citation considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with any communication.

Form PTO-1449	U.S. Department of Commerce Patent and Trademark Office	Atty. Docket No. 02-728-B	Serial No. 10/607,933
INFORMATION DISCLOSURE O I STATEMENT BY APPLICANT		Applicant: McSwiggen, et al.	
		Filing Date: June 27, 2003	Group:
			

	Amyloid Precursor Protein by a Disintegrin Metalloprotease," <u>PNAS</u> 96:3922-3927 (1999)
163.	Lasic and Needham "The 'Stealth' Liposome: A Prototypical Biomaterial," <u>Chemical Reviews</u> 95:2601-2627 (1995)
164.	Lasic and Papahadjopoulos, "Liposomes Revisited," <u>Science</u> 267:1275-1276 (1995)
165.	Lee and Larson, "Modified Liposome Formulations for Cytosolic Delivery of Macromolecules," <u>ACS Symposium Series</u> 752:184-192 (2000)
166.	Lee and Lee, "Preparation of Cluster Glycosides of N-Acetylgalactosamine That Have Subnanomolar Binding Constants Towards the Mammalian Hepatic Gal/GalNAc-specific Receptor," <u>Glyconjugates J.</u> 4:317-328 (1987)
167.	Lee et al., "Expression of Small Interfering RNA's Targeted Against HIV-1 rev Transcripts in Human Cells," <u>Nature Biotechnology</u> 19:500-505 (2002)
168.	L'Huillier et al., "Cytoplasmic Delivery of Ribozymes Leads to Efficient Reduction in α -Lactalbumin mRNA Levels in C1271 Mouse," <u>EMBO J.</u> 11:4411-4418 (1992)
169.	Lieber et al., "Stable High-Level Gene Expression in Mammalian Cells by T7 Phage RNA Polymerase," <u>Methods Enzymol.</u> 217:47-66 (1993)
170.	Limbach et al., "Summary: the modified nucleosides of RNA," <u>Nucleic Acids Research</u> 22(12):2183-2196 (1994)
171.	Lin and Matteucci, "A Cytosine Analogue Capable of Clamp-Like Binding to a Guanine in Helical Nucleic Acid," <u>J. Am. Chem. Soc.</u> 120:8531-8532 (1998)
172.	Lisziewicz et al., "Inhibition of Human Immunodeficiency Virus Type 1 Replication by Regulated Expression of a Polymeric Tat Activation Response RNA Decoy as a Strategy for Gene Therapy in AIDS," <u>Proc. Natl. Acad. Sci. U.S.A.</u> 90:8000-8004 (1993)
173.	Liu et al., "Cationic Liposome-mediated Intravenous Gene Delivery," <u>J. Biol. Chem.</u> 270(42):24864-24870 (1995)
174.	Loakes, "The Applications of Universal DNA Base Analogues," <u>Nucleic Acids Research</u> 29:2437-2447 (2001)
175.	Ma et al., "Design and Synthesis of RNA Miniduplexes via a Synthetic Linker Approach. 2. Generation of Covalently Closed, Double-Stranded Cyclic HIV-1 TAR RNA Analogs with High Tat-Binding Affinity," <u>Nucleic Acids Research</u> 21:2585-2589 (1993)
176.	Ma et al., "Design and Synthesis of RNA Miniduplexes via a Synthetic Linker Approach," <u>Biochemistry</u> 32:1751-1758 (1993)
177.	Martinez et al., "Single-Stranded Antisense siRNAs Guide Target RNA Cleavage in

Examiner	Date Considered

EXAMINER: Initial if citation considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with any communication.

Form PTO-1449 INFORMATION DISCLOSURE STATEMENT BY APPLICANT <i>OCT 1 2003 NOV 07 2003 PATENT & TRADEMARK OFFICE</i>	U.S. Department of Commerce Patent and Trademark Office	Atty. Docket No. 02-728-B	Serial No. 10/607,933
		Applicant: McSwiggen, et al.	
		Filing Date: June 27, 2003	Group:

	RNAi," <i>Cell</i> 110:563-574 (2002)
178.	Maurer et al., "Lipid-based systems for the intracellular delivery of genetic drugs," <i>Molecular Membrane Biology</i> 16:129-140 (1999)
179.	McCurdy et al., "Deoxyoligonucleotides with Inverted Polarity: Synthesis and Use in Triple-Helix Formation" <i>Nucleosides & Nucleotides</i> 10:287-290 (1991)
180.	McGarry and Lindquist, "Inhibition of heat shock protein synthesis by heat-inducible antisense RNA," <i>Proc. Natl. Acad. Sci. USA</i> 83:399-403 (1986)
181.	McManus et al., "Gene Silencing Using Micro-RNA Designed Hairpins," <i>RNA</i> 8:842-850 (2002)
182.	Mesmaeker et al, "Novel Backbone Replacements for Oligonucleotides," <i>American Chemical Society</i> , pp. 24-39 (1994)
183.	Miyagashi and Taira, "U6 Promoter-driven siRNAs with Four Uridine 3' Overhangs Efficiently Suppress Targeted Gene Expression in Mammalian Cells," <i>Nature Biotechnology</i> 19:497-500 (2002)
184.	Moore and Sharp, "Site-Specific Modification of Pre-mRNA: The 2'-Hydroxyl Groups at the Splice Sites," <i>Science</i> 256:992-996 (1992)
185.	Noonberg et al., <i>In vivo</i> generation of highly abundant sequence-specific oligonucleotides for antisense and triplex gene regulation," <i>Nucleic Acids Research</i> 22(14):2830-2836 (1994)
186.	Novina et al., "siRNA-Directed Inhibition of HIV-1 Infection," <i>Nature Medicine</i> 1-6 (2002)
187.	Nykanen et al., "ATP Requirements and Small Interfering RNA Structure in the RNA Interference Pathway," <i>Cell</i> 107:309-321 (2001)
188.	Ohkawa et al., "Activities of HIV-RNA Targeted Ribozymes Transcribed From a 'Shot-Gun' Type Ribozyme-trimming Plasmid," <i>Nucleic Acids Symp. Ser.</i> 27:15-16 (1992)
189.	Ojwang et al., "Inhibition of Human Immunodeficiency Virus Type 1 Expression by a Hairpin Ribozyme," <i>Proc. Natl. Acad. Sci. USA</i> 89:10802-10806 (1992)
190.	Oku et al., "Real-time analysis of liposomal trafficking in tumor-bearing mice by use of positron emission tomography," <i>Biochimica et Biophysica Acta</i> 1238:86-90 (1995)
191.	Ono et al., "DNA Triplex Formation of Oligonucleotide Analogs Consisting of Linker Groups and Octamer Segments That Have Opposite Sugar-Phosphate Backbone Polarities," <i>Biochemistry</i> 30:9914-9921 (1991)
192.	Pardridge et al., "Vector-mediated delivery of a polyamide ("peptide") nucleic acid analogue through the blood-brain barrier <i>in vivo</i> ," <i>Proc. Natl. Acad. Sci. USA</i>

Examiner	Date Considered

EXAMINER: Initial if citation considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with any communication.

Form PTO-1449	U.S. Department of Commerce Patent and Trademark Office	Atty. Docket No. 02-728-B	Serial No. 10/607,933
INFORMATION DISCLOSURE STATEMENT BY APPLICANT		Applicant: McSwiggen, et al.	
		Filing Date: June 27, 2003	Group:

NOV 07 2003

	92:5592-5596 (1995)
193.	Parrish, "Functional Anatomy of a dsRNA Trigger: Differential Requirement for the Two Trigger Strands in RNA Interference," <u>Molecular Cell</u> 6:1077-1087 (2000)
194.	Paul et al., "Effective Expression of Small Interfering RNA in Human Cells," <u>Nature Biotechnology</u> 20:505-508 (2002)
195.	Perreault et al., "Mixed Deoxyribo- and Ribo-Oligonucleotides with Catalytic Activity," <u>Nature</u> 344:565-567 (1990) (often mistakenly listed as Perrault)
196.	Pieken et al., "Kinetic Characterization of Ribonuclease-Resistant 2'-Modified Hammerhead Ribozymes," <u>Science</u> 253:314-317 (1991)
197.	Ponpipom et al., "Cell-Specific Ligands for Selective Drug Delivery to Tissues and Organs," <u>J. Med. Chem.</u> 24:1388-1395 (1981)
198.	Reinhart and Bartel, "Small RNAs Correspond to Centromer Heterochromatic Repeats," <u>Science</u> 297:1831 (2002)
199.	Reinhart et al., "MicroRNAs in Plants," <u>Genes & Development</u> 16:1616-1626 (2002)
200.	Richardson and Schepartz, "Tethered Oligonucleotide Probes. A Strategy for the Recognition of Structured RNA," <u>J. Am. Chem. Soc.</u> 113:5109-5111 (1991)
201.	Saenger (ed), "Modified Nucleosides and Nucleotides; Nucleoside Di- and Triphosphates; Coenzymes and Antibiotics, (ch.7)" <u>Principles of Nucleic Acid Structure</u> 158-200 (1984)
202.	Seaver et al., "Ribozymes as Potential Anti-HIV-1 Therapeutic Agents" <u>Science</u> 247:1222-1225 (1990)
203.	Scanlon et al., "Ribozyme-Mediated Cleavage of c-fos mRNA Reduces Gene Expression of DNA Synthesis Enzymes and Metallothionein," <u>Proc. Natl. Acad. Sci. USA</u> 88:10591-10595 (1991)
204.	Scaringe et al., "Chemical synthesis of biologically active oligoribonucleotides using β -cyanoethyl protected ribonucleoside phosphoramidites," <u>Nucl. Acids Res.</u> 18:5433-5441 (1990)
205.	Schroeder et al., "Diffusion Enhancement of Drugs by Loaded Nanoparticles in Vitro," <u>Pro. Neuro-Psychopharmacol. & Biol. Psychiat.</u> 23:941-949 (1999) [sometimes cited by RPI as <i>Prog Neuropsychopharmacol Biol Psychiatry</i> 23:941-949, 1999]
206.	Schwarz et al., "Evidence that siRNAs Function as Guides, Not Primers, in the <i>Drosophila</i> and Human RNAi Pathways," <u>Molecular Cell</u> 10:537-548 (2002)
207.	Seela and Kaiser, "Oligodeoxyribonucleotides containing 1,3-propanediol as nucleoside substitute," <u>Nucleic Acids Research</u> 15:3113-3129 (1987)
208.	Seela and Kaiser, <u>Nucleic Acids Res.</u> 1990, 18:6353

Examiner

Date Considered

EXAMINER: Initial if citation considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with any communication.

Form PTO-1449

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10/607,933

**INFORMATION DISCLOSURE
O STATEMENT BY APPLICANT**

NOV 07 2003

Applicant: McSwiggen, et al.

Filing Date:

June 27, 2003

Group:

	209.	Shabarova et.al., "Chemical ligation of DNA: The first non-enzymatic assembly of a biologically active gene," <u>Nucleic Acids Research</u> 19:4247-4251 (1991)
	210.	Sullenger and Cech, "Tethering Ribozymes to a Retroviral Packaging Signal for Destruction of Viral RNA," <u>Science</u> 262:1566-1569 (1993)
	211.	Sun, "Technology evaluation: SELEX, Giliad Sciences Inc," <u>Current Opinion in Molecular Therapeutics</u> 2:100-105 (2000)
	212.	Taira et al., "Construction of a novel RNA-transcript-trimming plasmid which can be used both <i>in vitro</i> in place of run-off and (G)-free transcriptions and <i>in vivo</i> as multi-sequences transcription vectors," <u>Nucleic Acids Research</u> 19:5125-5130 (1991)
	213.	Thompson et al., "Improved accumulation and activity of ribozymes expressed from a tRNA-based RNA polymerase III promoter," <u>Nucleic Acids Research</u> 23:2259-2268 (1995)
	214.	Turner et al., "Improved Parameters for Prediction of RNA Structure," <u>Cold Spring Harbor Symposia on Quantitative Biology</u> Volume LII, pp. 123-133 (1987)
	215.	Turner et al., "Free Energy Increments for Hydrogen Bonds in Nucleic Acid Base Pairs," <u>J. Am. Chem. Soc.</u> 109:3783-3785 (1987)
	216.	Tuschl et al., "Targeted mRNA Degradation by Double-Stranded RNA In Vitro," <u>Genes & Development</u> 3191-3197 (1999)
	217.	Tuschl, "RNA Interference and Small Interfering RNAs," <u>Chembiochem</u> 2:239-245 (2001)
	218.	Tyler et al., "Peptide nucleic acids targeted to the neurotensin receptor and administered i.p. cross the blood-brain barrier and specifically reduce gene expression," <u>Proc. Natl. Acad. Sci. USA</u> 96:7053-7058 (1999)
	219.	Tyler et al., "Specific gene blockade shows that peptide nucleic acids readily enter neuronal cells <i>in vivo</i> ," <u>FEBS Letters</u> 421:280-284 (1998)
	220.	Usman and Cedergren, "Exploiting the chemical synthesis of RNA," <u>TIBS</u> 17:334-339 (1992)
	221.	Usman et al., "Automated Chemical Synthesis of Long Oligoribonucleotides Using 2'-O-Silylated Ribonucleoside 3'-O-Phosphoramidites on a Controlled-Pore Glass Support: Synthesis of a 43-Nucleotide Sequence Similar to the 3'-Half Molecule of an <i>Escherichia coli</i> Formylmethionine tRNA," <u>J. Am. Chem. Soc.</u> 109:7845-7854 (1987)
	222.	Usman et al., "Chemical modification of hammerhead ribozymes: activity and nuclease resistance," <u>Nucleic Acids Symposium Series</u> 31:163-164 (1994)
	223.	Vassar et al., "β-Secretase Cleavage of Alzheimer's Amyloid Precursor Protein by the Transmembrane Aspartic Protease BACE," <u>Science</u> 286:735-741 (1999)

Examiner

Date Considered

EXAMINER: Initial if citation considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with any communication.

Form PTO-1449

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02-728-B

10/607,933

**INFORMATION DISCLOSURE
STATEMENT BY APPLICANT**

NOV 07 2003

Applicant: McSwiggen, et al.

Filing Date:
June 27, 2003

Group:

224.	Ventura et al., "Activation of HIV-Specific Ribozyme Activity by Self-Cleavage," <u>Nucleic Acids Research</u> 21:3249-3255 (1993)
225.	Verma and Eckstein, "Modified Oligonucleotides: Synthesis and Strategy for Users," <u>Annu. Rev. Biochem.</u> 67:99-134 (1998)
226.	Volpe et al., "Regulation of Heterochromatic Silencing and Histone H3 Lysine-9 Methylation by RNAi," <u>Science</u> 297:1833-1837 (2002)
227.	Weerasinghe et al., "Resistance to Human Immunodeficiency Virus Type 1 (HIV-1) Infection in Human CD4 ⁺ Lymphocyte-Derived Cell Lines Conferred by Using Retroviral Vectors Expressing an HIV-1 RNA-Specific Ribozyme," <u>Journal of Virology</u> 65:5531-5534 (1991)
228.	Wianny and Zernicka-Goetz et al., "Specific Interference with Gene Function by Double-Stranded RNA in Early Mouse Development," <u>Nature Cell Biology</u> 2:70-75 (2000)
229.	Wincott et al., "Synthesis, deprotection, analysis and purification of RNA and ribozymes," <u>Nucleic Acids Research</u> 23(14):2677-2684 (1995)
230.	Wincott et al., "A Practical Method for the Production of RNA and Ribozymes," <u>Methods in Molecular Biology</u> 74:59-69 (1997)
231.	Wolfe et al., "Two Transmembrane Aspartates in Presenilin-1 Required for Presenilin Endoproteolysis and γ -Secretase Activity," <u>Nature</u> 398:513-517 (1999)
232.	Wu and Wu, "Receptor-mediated <i>in Vitro</i> Gene Transformation by a Soluble DNA Carrier System," <u>The Journ. of Biol. Chem.</u> 262:4429-4432 (1987)
233.	Yu et al., "A Hairpin Ribozyme Inhibits Expression of Diverse Strains of Human Immunodeficiency Virus Type 1," <u>Proc. Natl. Acad. Sci. USA</u> 90:6340-6344 (1993)
234.	Zamore et al., "RNAi: Double-Stranded RNA Directs the ATP-Dependent Cleavage of mRNA at 21 to 23 Nucleotide Intervals," <u>Cell</u> 101:25-33 (2000)
235.	Zhou et al., "Synthesis of Functional mRNA in Mammalian Cells by Bacteriophage T3 RNA Polymerase," <u>Mol. Cell. Biol.</u> 10:4529-4537 (1990)

Examiner

Date Considered

EXAMINER: Initial if citation considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with any communication.